Cell Autonomous Role of PTEN in Regulating Castration-Resistant Prostate Cancer Growth.

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Public Summary:
Alteration of the PTEN/PI3K pathway is associated with late-stage and castrate-resistant prostate cancer (CRPC). However, how PTEN loss is involved in CRPC development is not clear. Here, we show that castration-resistant growth is an intrinsic property of Pten null prostate cancer (CaP) cells, independent of cancer development stage. PTEN loss suppresses androgen-responsive gene expressions by modulating androgen receptor (AR) transcription factor activity. Conditional deletion of Ar in the epithelium promotes the proliferation of Pten null cancer cells, at least in part, by downregulating the androgen-responsive gene Fkbp5 and preventing PHLPP-mediated AKT inhibition. Our findings identify PI3K and AR pathway crosstalk as a mechanism of CRPC development, with potentially important implications for CaP etiology and therapy.

Scientific Abstract:
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